

Lactic Acidosis in Children – A Varied Presentation

Ira Shah¹

¹ Department of Pediatrics, B J Wadia Hospital for Children, Mumbai, India

Address for correspondence Ira Shah, MD, 1/B Saguna, 271/B St Francis Road, Vile Parle West, Mumbai 400056, India (e-mail: irashah@pediatriconcall.com).

J Pediatr Intensive Care 2017;6:206–208.

Abstract

Primary lactic acidemias represent a family of disorders of pyruvate metabolism or defects in the respiratory chain. However, lactic acidosis may also be seen in metabolic disorders such as organic acidemias, urea cycle defects, and fatty acid oxidation defects, which can be easily excluded by serum ammonia estimation, urinary organic acid estimation, and quantification of plasma amino acids. The classical presentation of a patient with primary lactic acidemia is growth retardation, ataxia, stroke, and increased lactic acid levels in the blood and cerebrospinal fluid. Patients may also present with cerebral edema, acute rhabdomyolysis, cardiac arrhythmias, cardiomyopathy, coma, and neurodegeneration. We present three cases of lactic acidemia with varied presentation. The first child presented at 5 years with recurrent hematemesis with hypoglycemia. The second child presented at 11 years of age with recurrent episodes of unconsciousness. The third child presented at one and a half months with convulsions.

Keywords

- lactic acidosis
- children
- presentation

Introduction

Metabolic disorders in infants classically present with poor feeding, lethargy, vomiting, and failure to thrive with convulsions or coma. In older children and adults, patients may present with cerebral edema, acute rhabdomyolysis, cardiac arrhythmias, cardiomyopathy, coma with lactic acidosis, strokelike episodes, ataxia, and neurodegeneration.^{1,2} Among the lactic acidemias, pyruvate metabolism defects present in the first 48 hours of life. These disorders are typically nuclear encoded subunits of the mitochondrial respiratory chain complex and appear in newborns and infants, whereas mitochondrial DNA disorders occur commonly in adults and older children. We present three children who had a varied presentation of inherited metabolic disorders, though all had lactic acidemia.

Case 1

A five-year old male child born of nonconsanguineous marriage presented with repeated episodes of hematemesis since 6 months of age and fever since 5 days. At 2 years of age, he had hematemesis with hepatic encephalopathy and was diagnosed to be Hepatitis A IgM positive. He was treated with fresh frozen

plasma and packed red blood cell transfusion. An esophageo-gastroscopy revealed gastritis. At 2½ years of age, he had vomiting, fever, and hematemesis associated with altered sensorium. He had persistent hepatic dysfunction with elevated serum transaminases and had severe metabolic acidosis. His cerebrospinal fluid (CSF) analysis, serum electrolytes, and CT brain were normal. His liver biopsy showed normal architecture of the liver with vacuolar changes, focal steatosis, and Kupffer cell hyperplasia with mild chronic periportal inflammation. He was treated with bicarbonate infusions. At 4 years of age, he had generalized tonic clonic convulsions. His liver function tests were normal, and he was noted to have hypoglycemia with metabolic acidosis. He was treated with glucose and bicarbonate infusions. At 4½ years of age, he had vomiting along with hematemesis. His liver function tests were normal, and he had severe metabolic acidosis with hypoglycemia. His barium swallow was normal. He was treated with bicarbonate infusions and packed red blood cell transfusion. At 4¾ years of age, he presented again with hematemesis and had hypoglycemia with prolonged prothrombin time. His urine ketones were positive, and he was treated with fresh frozen plasma and glucose infusions. His various biochemical pictures are depicted in ► **Table 1**.

received

April 19, 2016

accepted after revision

October 22, 2016

published online

December 1, 2016

Copyright © 2017 by Georg Thieme
Verlag KG, Stuttgart · New York

DOI <https://doi.org/10.1055/s-0036-1596065>.
ISSN 2146-4618.

Table 1 Biochemical abnormalities of Case 1 over a period of 3 years

Age of presentation	2 years	2½ years	4 years	4½ years	4¾ years	5 years
SGOT (IU/l)	2055	357	46	104	—	170
SGPT (IU/l)	501	267	24	43	—	78
S. Ammonia (mg/dl)	53	—	—	—	—	90
S. Bilirubin (mg%)	4.1	0.5	0.9	0.6	—	0.5
Serum alkaline phosphatase (IU/L)	551	248	158	151	—	154
Prothrombin Time (sec)	13	11.2	—	—	18.2	—
Partial Thromboplastin Time (sec)	40	34.4	—	—	60	—
Random Serum glucose (mg/dl)	53	67	10	10	12	40
pH	7.1	6.9	7.2	6.9	—	6.9
Bicarbonate (mmol/L)	5.2	3.8	11.3	3.5	—	2.8
Total proteins (gm/dl)	4.8	—	4.6	4.1	—	4.3

On presentation, the child had acidotic breathing with respiratory rate of 62/min. He had a mild hepatomegaly, though other examination findings were normal. His investigations revealed severe metabolic acidosis (pH = 6.91, bicarbonate = 2.8 mmol/L) with positive anion gap (30) with hypoglycemia (RBS = 40 mg %). His liver transaminases were elevated (SGOT = 170 IU/L, SGPT = 78 IU/L) and other liver function tests and hemogram were normal. He was suspected as a case of metabolic disorder with metabolic acidosis, hypoglycemia, and chronic liver disease. His serum lactate was elevated [37.4 mg/dl (Normal 5.7–22 mg/dl)] and serum pyruvate was normal [0.55 mg/dl (Normal = 0.36–0.59 mg/dl)] with an elevated lactate: pyruvate ratio of 68. His urine organic acids chromatography and serum carnitine was normal. His serum ANA, ds DNA, ceruloplasmin, ultrasound of abdomen, serum ammonia, serum creatine phosphokinase, urinary copper were all normal. His HIV, HBsAg, and anti-HCV ELISA were negative. Thus, he was diagnosed as a case of lactic acidosis with recurrent hematemesis, hypoglycemia, and chronic liver disease. He was treated with bicarbonate infusions, IV antibiotics and glucose infusions and discharged on supplements of Coenzyme Q, Carnitine, Thiamine, and Riboflavin. On follow-up after 6 months, he was asymptomatic.

Case 2

An eleven-year-old boy born of nonconsanguineous marriage presented with recurrent episodes of fever associated with loss of consciousness since 3 years. He also had breathlessness on exertion since 3 years. He had a first episode of fever with altered sensorium 3 years prior to presentation, for which he was admitted in a private hospital and diagnosed as viral encephalitis though CSF and CT brain done were normal. He recovered normally during this episode. Two and a half years prior to presentation, he had bilious vomiting and an exploratory laprotomy was performed that showed malrotation. One year prior to presentation, he was admitted with tetanic spasms and diagnosed to have hypocalcemic convulsions. One month prior to presentations, he was admitted with

fever, hematemesis, and one episode of uprolling of eye ball. An esophageogastroscopy was performed, which showed gastritis. He had two elder brothers who were asymptomatic. His developmental milestones were normal. On examination, there were no positive findings. In view of recurrent episodes of unconsciousness with breathlessness on exertion, he was suspected to have an underlying metabolic disorder. His venous blood gas, random serum glucose, serum ammonia, liver enzymes were normal. His blood lactate was elevated [56.9 mg/dl] and blood pyruvate was decreased [0.1 mg/dl] with a lactate: Pyruvate ratio was 569. His CSF lactate was also elevated [23.9 mg/dl] with CSF pyruvate of 0.2 mg/dl. His urinary organic acids and quantification of plasma amino acids were normal. His blood galactosidase and arylsulfatase levels were normal. Muscle biopsy was noncontributory and did not show any evidence of mitochondrial myopathy. Serum carnitine levels were normal. EEG was done in view of convulsion, which was also normal. Thus, this child was diagnosed as a case of lactic acidosis with recurrent decompensation with stress causing transient encephalopathy and even gastritis. He was started on thiamine, riboflavin, and coenzyme Q supplements. He was advised regular follow-up.

Case 3

A one and a half month old male child born of third degree consanguineous marriage presented with myoclonic convulsions since the age of 10 days. He had two elder siblings, both males who had similar episodes of convulsions at 4 months age and had died at 5 years and 3 years, respectively. On examination, there were no positive findings. In view of similar episodes in older siblings, an inborn error of metabolism was considered.

His serum glucose, serum calcium, phosphorus, alkaline phosphatase, serum ammonia, and serum electrolytes were all normal. His venous blood gas revealed metabolic acidosis with positive anion gap (pH = 7.09, HCO₃ = 12.3 mmol/L and anion gap = 23). In view of the metabolic acidosis, a CSF lactate was done, which was elevated [27.3 mg/dl]

(Normal = 10.8 to 18.9 mg/dl)] with simultaneous elevated serum lactate and normal pyruvate [S. lactate = 66 mg/dl, S. pyruvate = 0.4 mg/dl] and elevated lactate: pyruvate ratio (160). His MRI brain was normal and EEG was grossly abnormal. His urinary organic acids revealed lactic aciduria. Thus, he was diagnosed as a case of lactic acidosis and started on thiamine, riboflavin, coenzyme Q, carnitine, and pyridoxine supplements and advised regular follow-up.

Discussion

Primary lactic acidemias occur either due to disorders of pyruvate metabolism or due to defects in respiratory chain. Primary lactic acidemia is seen with defects in gluconeogenesis where conversion of pyruvate to glucose is interrupted, and with mitochondrial enzyme defects. These patients present with episodes of hypoglycemia and life-threatening metabolic acidosis as was seen in our first patient.³ Definitive diagnosis of these defects in gluconeogenesis is established by enzyme analysis in liver or lymphocytes or molecular genetic testing, which we were unable to do in our patient due to unavailability of the facility. Treatment of acute attacks consists of correction of hypoglycemia and acidosis by intravenous glucose and bicarbonate infusions as we did in our first patient who had recurrent episodes of hypoglycemia and lactic acidosis and avoiding prolonged periods of fasting.

Patients with defects in pyruvate metabolism may present in the neonatal period with lethal lactic acidosis and white matter cystic lesions, and older children may present with ataxia. In addition, patients with holocarboxylase synthetase deficiency or biotinidase deficiency may have alopecia and rash. Our second patient presented at an older age with repeated episodes of fainting though he had no ataxia and also his muscle biopsy did not show any mitochondrial myopathy suggestive that most likely his lactic acidemia was due to defects in pyruvate metabolism. Enzyme analysis in liver or skin fibroblasts is confirmatory, which we were unable to do due to unaffordability in our patient. Treatment with thiamine and riboflavin has been found useful³ that we have initiated in our patient.

Defects in mitochondrial respiratory chain lead to a varied clinical presentation and skeletal muscle and heart are usually involved. Patients may present with infantile myopathies such as MELAS (mitochondrial encephalopathy, myopathy, lactic acidosis and stroke-like episodes), MERRF (myoclonus epilepsy, with ragged red fibers) and Kearns-Sayre syndrome (external ophthalmoplegia, acidosis, retinal degeneration, heart block, myopathy). Our third patient had presented with myoclonic epilepsy and had other siblings who had died due to same problems. Though measurement of enzyme activity in tissues or analysis of mitochondrial DNA mutation can confirm the particular defect, we were unable to do in our third patient due to unavailability of facility. In patients with mitochondrial defects, replacement with coenzyme Q, carnitine, riboflavin, nicotinamide has been found beneficial,³ which we have supplemented in our patient. Also an elevated lactate: pyruvate ratio is suggestive of mitochondrial respiratory chain defect or pyruvate carboxylase Type B deficiency³ as was seen in both our second and third patient. However, in second patient, muscle biopsy did not reveal any evidence of myopathy.

In conclusion, we have three patients presenting in three different age groups with different clinical presentations of lactic acidemia due to defects in different pathways namely that of gluconeogenesis, defect in pyruvate metabolism, and defect of respiratory enzyme chain. Thus, in a child with unexplained metabolic acidosis with elevated anion gap with normal plasma amino acids, serum ammonia, and normal urine organic acids, lactic acidemia should be suspected.

References

- 1 Hoffman GF, Nyhan WL, Zschocke J, Kahler SA, Mayatepek E. Inherited Metabolic Disorders. In: Core Handbooks in Pediatrics. Philadelphia: Lippincott Williams & Wilkins; 2002:39–55
- 2 Burton BK. Inborn errors of metabolism in infancy: a guide to diagnosis. *Pediatrics* 1998;102(6):E69
- 3 Chen YT. Defects in intermediary carbohydrate metabolism associated with lactic acidosis. In: Behrman RE, Kliegman RM, Jenson HB, eds. *Nelson's Textbook of Pediatrics*. 17th ed. Philadelphia: Elsevier; 2004:477–480